Germany
[10]University Hospital Wuerzburg, Radiooncology, Wuerzburg, Germany

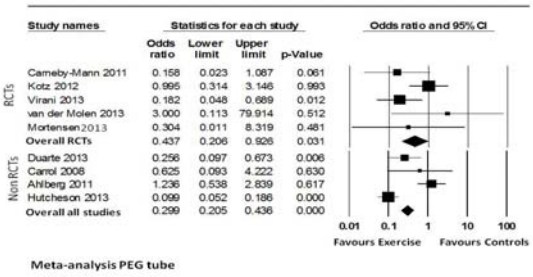
Purpose/Objective: In contrast to patients with early stage NSCLC, clear recommendations are still missing for SBRT for lung metastases regarding patient selection, planning, delivery, dose and quality assurance. This report of the German working group stereotactic radiotherapy pools SBRT patient data of German centers and aims to describe local control, overall survival, prognostic factors and dose recommendations in respect to the different primary subgroups.
Materials and Methods: All radiotherapy departments in Germany were contacted and invited to participate in this study. 700 patients with 963 lung metastases treated with SBRT were included in this database. The analyzed subgroups were NSCLC (25.7%), colorectal cancer (22.6%), renal cell cancer (6.7%), breast cancer (6.2%) and sarcoma. 30% of the lesions were treated as single fraction radiosurgery, 36% in a three fraction approach, 34% lesions with different fractionation.
Results: Median follow-up time was 26.4 months. For the entire patient cohort, an excellent local control rate after 1 year of 90.8% and after 2 years of 81.4% was detected. In detail, the best 1-year- and 2-year-local control rate was achieved for breast cancer (97.5% vs. 97.5%), followed by renal cell carcinoma (96.2% vs. 93.3%), NSCLC (94.7% vs. 76.2%), colorectal cancer (88.3% vs. 81.2%) and sarcoma (68.7% vs. 45.8%). For the entire patient cohort, local control was significantly influenced by primary tumor histology, Karnofsky performance scale, localization (central vs. peripheral), time of metastases detection (synchronous vs. metachronous) and maximum tumor diameter. 2-year overall survival rates were 64.5% for breast cancer, 66.1% for colorectal cancer, 62.7% for renal cell carcinoma, 54.7% for NSCLC and 39.1% for sarcoma. Additionally, conducting biological modeling we tried to propose primary specific dose recommendations needed for 90%-2-year-local control for the different tumor entities (e.g. BED= 97.5 Gy for NSCLC vs. BED = 108.8 Gy for colorectal cancer).
Conclusions: SBRT for lung metastases from different primary tumors was effective and safe despite considerable interinstitutional variability in SBRT practice throughout Germany. Prognostic factors and doses for 90%-local control are truly dependent on the different primary tumors. Future prospective studies are of highly interest to evaluate dose recommendations and prognostic factors.

OC-0057

Meta-analysis of prophylactic swallowing exercises in head and neck radiotherapy

H.R. Mortensen[1], K. Jensen[1], C. Grau[1]
[1]Aarhus University Hospital, Oncology, Aarhus C, Denmark

Purpose/Objective: Many head and neck cancer survivors experience reduced quality of life due to radiotherapy-related dysphagia and swallowing exercises have been suggested as an option for treatment hereof. The aim of this meta-analysis was to evaluate the impact of prophylactic swallowing exercises on swallowing-related outcomes in head and neck patients treated with curative radiotherapy.
Materials and Methods: Pubmed was searched for publications up to Oct 30th 2014 on subject headings for the following concepts: swallowing exercises, dysphagia rehabilitation, radiotherapy and head and neck cancer; all reference lists in the selected journal articles were additionally screened for potentially relevant articles. Included papers contained information on objective endpoints (N=4), observer-rated endpoints (N=8), patient-rated endpoints (N=5), clinical endpoints (N=10) or a combination of these. A meta-analysis of PEG tube incidence was performed using 'Comprehensive Meta-analysis'; a p value ≤ 0.05 was considered significant.
Results: A total of 12 papers were included. In general, most of the studies reported some positive results of swallowing therapy but a comparison was complicated by the broad range of interventions, evaluation times and endpoints used and the benefit was not consistent and not related to specific measures.
Incidence of PEG tube was the endpoint most often reported (N=9) and the only endpoint suited for meta-analysis. In the current setting, four studies reported a benefit from prophylactic exercises and five studies reported no difference on PEG tube incidence. A meta-analysis of these studies regardless of evaluation time and design (Figure 1) showed an overall benefit of prophylactic exercises with an odds ratio of 0.30 (95% CI: 0.21-0.44). This benefit remained if only randomized controlled trials (RCTs) or studies examining incidence of tube feeding ≥ 6 months post-treatment was used.



Conclusions:
The meta-analysis showed a positive impact of prophylactic swallowing exercises on PEG tube incidence; it was not possible to examine other endpoints in this meta-analysis due to heterogeneous use of evaluation methods and scales.

OC-0058

SIB-IMRT in patients with < 5 brain metastases: phase I trial final results (ISIDE-BM-1)

G. Macchia[1], M. Ferro[1], F. Deodato[1], S. Cilla[2], M. Nuzzo[1], L. Caravatta[1], S. Mignogna[3], S. Cammelli[4], V. Valentini[5], A.G. Morganti[4]
[1]Fondazione "Giovanni Paolo II" Catholic University of Sacred Heart, Radiation Oncology Unit, Campobasso, Italy
[2]Fondazione "Giovanni Paolo II" Catholic University of Sacred Heart, Medical Physics Unit, Campobasso, Italy
[3]Fondazione "Giovanni Paolo II" Catholic University of Sacred Heart, Oncology Unit, Campobasso, Italy
[4]Policlinico Universitario S. Orsola-Malpighi, Radiotherapy Department, Bologna, Italy
[5]"A. Gemelli" Hospital Catholic University of Sacred Heart, Radiotherapy Department, Rome, Italy

Purpose/Objective: To determine the maximum tolerated dose (MTD) of an hypofractionated accelerated IMRT treatment with the simultaneous integrated boost (SIB) technique in patients with ≤ 5 brain metastases.
Materials and Methods: Patients with ≤ 5 brain metastases and no extra-cranial disease were enrolled in a phase I study. IMRT was delivered over 2 weeks in 10 fractions to the two planning target volumes (PTVs) defined by adding 5-mm margin to the respective clinical target volumes (CTVs). The CTV1 was defined as each single lesion (GTV) on the basis of

the contrast-enhanced MRI imaging. CTV2 encompassed the whole brain. Only the PTV1 dose was escalated (planned dose escalation: 35 Gy, 40 Gy, 45 Gy, 50 Gy) while the PTV2 dose remained the same (30 Gy/3 Gy/fractions). Dose-limiting toxicities (DLTs) were defined as any treatment-related non-hematological adverse effects rated as grade ≥ 3, or any hematological toxicity rated as ≥ 4 by CTCAE scale, v. 4.0. MTD was exceeded if ≥ 2 of 6 patients in a cohort experienced dose-limiting toxicity (DLT).

Results: 27 consecutive patients (pts) were treated (PTV1 dose: 35 Gy, 8 pts; 40 Gy, 6 pts; 45 Gy, 6 pts; 50 Gy, 7 pts). The number of treated brain lesions was: 1 (17 pts), 2 (4 pts), 3 (5 pts) and 4 (1 pt). Three pts experienced a DLT: 1 pt (2nd dose level) developed a grade 3 skin toxicity, 1 pt had a grade 3 neurological toxicity (4th dose level) and 1 pt had a brain hemorrhage (4th dose level). Nineteen pts experienced cutaneous (17 pts) and/or neurological (10 pts) grade 1-2 acute toxicity. The response to treatment was evaluable in 16 pts: 1 pt (6.2%) disease progression, 2 pts (12.5%) stable disease, 10 pts (62.5%) partial response and 3 pts (18.8%) complete response. Median and 1-year overall survival were 13 months and 51.9%, respectively. Late toxicity was not recorded.

Conclusions: This is the first prospective trial demonstrating that a radiation dose of 50 Gy in 10 fractions can be delivered by using a SIB IMRT technique without unacceptable toxicity in patients with ≤ 5 brain metastases. A phase II trial (ISIDE-BM-2) is in progress to evaluate the response and the time to progression.

OC-0059

Validated clinical model for survival prediction after stereotactic radiotherapy for brain metastases

J. Zindler[1], R.J. Beumer[1], E.G.C. Troost[1], A.L. Hoffmann[1], I. Compter[1], J. Jager[1], D. Eekers[1], P. Lambin[1]

[1]MAASTRO Clinic, Radiotherapie, Maastricht, The Netherlands

Purpose/Objective: Stereotactic ablative body radiotherapy (SABR) is the standard treatment modality for a limited number of brain metastases (BM). Several models for survival prediction have been published, such as the commonly used Recursive Partitioning Analysis (RPA), Golden Grading System (GGS), and the Disease Specific Graded Partitioning Analysis (DS-GPA). All published models have limitations for prediction of survival after SABR for BM: e.g. small proportion of patients in the favorable prognostic group, a low sensitivity for the identification of patients with long term survival, and some models are complex to use (e.g. DS-GPA). In this study, a new prognostic model is developed with the aim of overcoming above mentioned limitations.

Materials and Methods: Based on published models and clinical practice a new prognostic model was developed. Its clinical utility was tested for prediction of early death (<3 months) and long term survival (>12 months) in 297 patients with 1 up to 4 newly diagnosed BM treated with Linac-based SABR at our department between July 2004 and July 2014. Prescribed dose at the edge of the PTV was in the range of 15 up to 24Gy in 1 or 3 fractions.

Results: In the published models the two most important prognostic factors were: WHO performance status and presence of extracranial metastases. Poor performance status only was identified as the poor prognostic group according to Dutch guidelines. Remaining patient cohort was divided based on the presence of extracranial metastases. The developed model is a simplified version of the commonly used RPA, and was named Simplified Recursive Partitioning Analysis (SRPA).

- SRPA class I: WHO performance status 0/1 & no extracranial metastases
- SRPA class II: WHO performance status 0/1 & extracranial metastases
- SRPA class III: WHO performance status of 2 or more

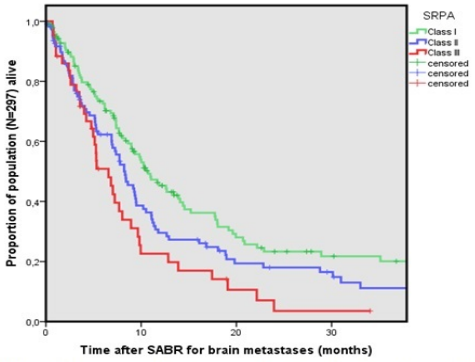
Median age was 63 years and the majority of patients had non-small cell lung cancer (64%). The median survival after SABR was 9 months, with 3 months-, 1 year-, and 5 years survival of respectively 81%, 36%, and 9%. The patient distribution was most balanced in the SRPA with 48% of patients in the favorable prognostic class (vs 20%-29% in the other models, Table 1). Sensitivity for prediction of long-term survival was highest using the SRPA (56% vs 16-46% in other classes). The specificity of predicting 3-months death in the poor prognostic class was high in all scores (range 86% up to 98%). The SRPA was valid in an external SABR for 1-3 BM patients data set.

Table: Clinical utility of prognostic models for prediction of early death or long term survival

	Prediction of early death <3 months in unfavorable classes						Prediction of long term survival (>12 months) in favorable classes					
	N (%)	OS (months)	Sensitivity	Specificity	PPV	NPV	N (%)	OS (months)	Sensitivity	Specificity	PPV	NPV
SRPA	43 (15%)	7	17%	86%	21%	83%	142 (48%)	11	56%	55%	31%	78%
RPA	43 (15%)	7	17%	86%	21%	83%	60 (20%)	11	16%	82%	35%	61%
GGS	8 (3%)	5	6%	98%	38%	83%	86 (29%)	11	21%	74%	34%	60%
DS-GPA	10 (4%)	9	9%	97%	40%	84%	54 (21%)	12	46%	85%	41%	68%

SRPA=simplified recursive partitioning analysis, RPA=recursive partitioning analysis, GGS=Golden Grading Scale, DS-GPA=disease specific Graded Partitioning Analysis, OS=overall survival, PPV=positive predictive value, NPV=negative predictive value

Figure Kaplan Meyer analysis of survival of the SRPA for three prognostic groups



SRPA=simplified recursive partitioning analysis, SABR=stereotactic ablative body radiotherapy

Conclusions: The SRPA had the highest clinical utility for survival prediction after SABR for BM compared to the RPA, DS-GPA, and GGS. The SRPA is very simple in use, assembles to clinical practice, has a balanced patient distribution between the favorable and intermediate group, the highest sensitivity for prediction of long term survival, was specific for prediction of early death, and was validated in an external population. Further research will focus on further validation in other BM populations and exploration of the predictive value of advanced techniques such as radiomics, biomarkers, and statistical modeling.

Joint Symposium: ESTRO-RANZCR: Imaging and tumour biology: Delivery

SP-0060

Image and biological guided adaptive radiotherapy; results from the ARTFORCE project

H. Bartelink[1], X. ARTFORCE Project Partners